1: J Clin Oncol 1990 May;8(5):856-69

Active-specific immunotherapy for melanoma.

Mitchell MS, Harel W, Kempf RA, Hu E, Kan-Mitchell J, Boswell WD, Dean G, Stevenson L.

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Twenty-five patients with metastatic melanoma were treated with a therapeutic vaccine ("theraccine") consisting of allogeneic melanoma lysates and a novel adjuvant, DETOX (Ribi ImmunoChem Research, Inc, Hamilton, MT). Each patient received 200 antigenic units (20 x 10(6) tumor cell equivalents) subcutaneously on weeks 1, 2, 3, 4, and 6. Clinical responses included one complete remission, three partial remissions, and a long-term (17-month) stability. Two other patients had mixed responses, with partial remissions of numerous subcutaneous nodules. Sites of responsive disease included primarily the skin, but ileal, breast, and a liver metastasis also responded. Removal of residual lesions in patients with partial remissions, whose other lesions had disappeared during treatment, led to long disease-free survivals. The median duration of remission was 17 months, with four of the five responders alive for at least 24 months after treatment. An increase in precursors of cytolytic T cells (CTLs) correlated with clinical outcome, when complete, partial, and mixed responses and long-term stability were considered. The CTLs recognized melanoma-associated antigens on many cell lines, but not other types of tumor or normal lymphocytes. Skin-test reactivity to melanoma antigens and serum antibodies against the melanoma cells was unrelated to clinical response. Toxicity was minimal, restricted largely to minor soreness at the site of injection. Only five patients, four of whom were treated with repeated courses, developed severe granulomas. These results confirm that active-specific immunization with allogeneic lysates of melanoma administered with the adjuvant DETOX can induce immunity to melanoma, and can induce regressions of disease in a proportion of patients with metastatic disease with little toxicity.

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1: Semin Surg Oncol 1993 May-Jun;9 (3):264-72

Interim results of a phase II multicenter clinical trial evaluating the activity of a therapeutic allogeneic melanoma vaccine (theraccine) in the treatment of disseminated malignant melanoma.

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A total of 139 patients with disseminated malignant melanoma were enrolled in an uncontrolled Phase II trial evaluating the activity of Melacine, allogeneic vaccine incorporating Detox, immunologic adjuvant. Nineteen patients, including 18 with progressive disease, dropped out of the study prior to receiving one full vaccination course of five injections over 6 weeks. Disease presentation among study participants included skin or lymph nodes (34%), pulmonary (24%), visceral (34%), and no evidence of disease (NED) (7%). One documented metastatic site was seen in 41%, two sites in 24%, and three or more sites in 27% of the patients studied. Objective clinical response rates for evaluable patients were CR 3%, PR 5%, minor response 4%, stable 23%, and progressive disease 65%. Median survival from time of diagnosis for patients treated with Melacine is presently estimated at 23 months (45/139 patients censored). Median date from diagnosis of metastatic disease to study entry was 3 months. Side effects were generally mild to moderate with pain at injection site (37%), granulomas (13%), erythema (6%), and flu-like symptoms (14-29%) predominating. Precursor antimelanoma cytotoxic T cell (pre-CTL) titers, in comparison with prestudy evaluations, clearly increased in 42% of the patients evaluated. Significantly extended survival characteristics were observed among patients who displayed an expansion of a population of CD57, CD8 co-positive lymphocytes during therapy in comparison with those patients not displaying this peripheral blood lymphocyte (PBL) population expansion (34 mo vs. 12 mo, respectively, $p = 0.04$) and among those patients displaying disease stabilization or better as a clinical response ($p = 0.001$).(ABSTRACT TRUNCATED AT 250 WORDS)

Publication Types:

1: Cancer Immunol Immunother 1996 Jul;42 (6):362-8

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Cancer Immunology Immunotherapy

Expression of human prostate-specific antigen (PSA) in a mouse tumor cell line reduces tumorigenicity and elicits PSA-specific cytotoxic T lymphocytes.

Wei C, Storozynsky E, McAdam AJ, Yeh KY, Tilton BR, Willis RA, Barth RK, Looney RJ, Lord EM, Frelinger JG.

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Human prostate-specific antigen (PSA) has a highly restricted tissue distribution. Its expression is essentially limited to the epithelial cells of the prostate gland. Moreover, it continues to be synthesized by prostate carcinoma cells. This makes PSA an attractive candidate for use as a target antigen in the immunotherapy of prostate cancer. As a first step in characterizing the specific immune response to PSA and its potential use as a tumor-rejection antigen, we have incorporated PSA into a well-established mouse tumor model. Line 1, a mouse lung carcinoma, and P815, a mouse mastocytoma, have been transfected with the cDNA for human PSA. Immunization with a PSA-expressing tumor cell line demonstrated a memory response to PSA which protected against subsequent challenge PSA-expressing, but not wild-type, tumors. Tumor-infiltrating lymphocytes could be isolated from PSA-expressing tumors grown in naive hosts and were specifically cytotoxic against a syngeneic cell line that expressed PSA. Immunization with tumor cells resulted in the generation of primary and memory cytotoxic T lymphocytes (CTL) specific for PSA. The isolation of PSA-specific CTL clones from immunized animals further demonstrated that PSA can serve as a target antigen for antitumor CTL. The immunogenicity studies carried out in this mouse tumor model provide a rationale for the design of methods to elicit PSA-specific cell-mediated immunity in humans.

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